Special Article

Endemic selenium intoxication of humans in China[1]

Guangqi Yang,[2] Shuzhen Wang,[3] Ruihua Zhou,[3] and Shuzhuang Sun[3]

ABSTRACT An endemic disease was discovered in 1961 in parts of the population of Enshi County, Hubei Province of the People's Republic of China. During the years of the highest prevalence, from 1961 to 1964, the morbidity was almost 50% in the 248 inhabitants of the five most heavily affected villages; its cause was determined to be selenium intoxication. The most common sign of the poisoning was loss of hair and nails. In areas of high incidence, lesions of the skin, nervous system, and possibly teeth may have been involved. A case is reported of a middle-aged, female hemiplegic, whose illness and death apparently were related to selenosis. Daily dietary intakes of selenium, estimated after the peak prevalence had subsided, averaged 4.99 (range 3.20 to 6.69) mg and hair and blood selenium levels averaged 32.2 and 3.2 μg/ml, respectively. Up to 1000× differences occurred when selenium contents of vegetables, cereals, scalp hair, blood, and urine from the selenosis areas were compared with those from Keshan disease (selenium deficiency) areas. The ultimate environmental source of selenium was a stony coal of very high selenium content (average more than 300 μg/g; one sample exceeded 80,000 μg/g). Selenium from the coal entered the soil by weathering and was available for uptake by crops because of the traditional use of lime as fertilizer in that region. This particular outbreak of human selenosis was due to a drought that caused failure of the rice crop, forcing the villagers to eat more high-selenium vegetables and maize and fewer protein foods. *Am J Clin Nutr* 1983;37:872–881.

KEY WORDS Selenium toxicity in man, human selenosis, seleniferous foods, endemic selenium poisoning

Introduction

The first description of an animal disease now known to be selenium poisoning was that of Marco Polo during his travels in West China in 1295, but subsequent reports of selenosis in China have not appeared. In Enshi County of Hubei Province **(Fig 1)** an endemic human disease of unknown origin, characterized by loss of hair and nails, appeared more than 20 yr ago (1) and reached a peak prevalence during the years 1961 to 1964. The average incidence in five heavy prevalence villages with 248 inhabitants was 49.2%. In the most severely affected village, incidence reached 82.5%, and only one elderly man of 82 yr and three breast-fed infants were unaffected. All residents were evacuated from their homes to nearby places of safety; they recovered as soon as their diets were changed, except those with symptoms of the nervous system who needed a longer time.

Research showed that the corn from this area was toxic. Because of a pink coloration in the tip of the corn embryo and of fungus spores in the seed, fungal intoxication was

[1] From the Department of Nutrition and Food Hygiene, Institute of Health, Chinese Academy of Medical Sciences, Beijing, People's Republic of China.

[2] Professor of Nutrition, Institute of Health Chinese Academy of Medical Science.

[3] Present address: Institute of Health, Chinese Academy of Medical Science 29 Han Wei Road, Beijing, China.

Received August 27, 1982.

Accepted for publication December 14, 1982.

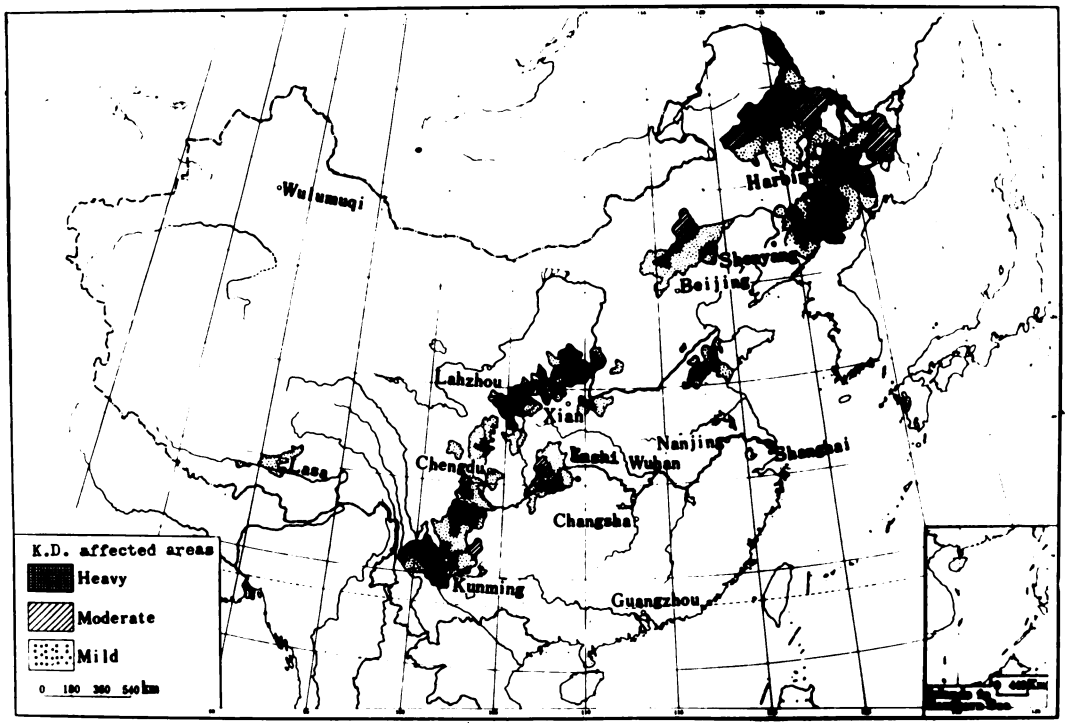

FIG 1. Distribution of Keshan Disease (KD) and location of endemic selenosis (Enshi county) in China. (The distribution of KD is after Tan Jianan, et al Acta Geograph Sinica 1979;34:85.)

suggested as the cause of the disease (Collaborative Group of Enshi Region, unpublished observations). Later work from our laboratory, however, demonstrated that the toxicant in the corn was selenium (1). The pink color indicated the presence of elemental selenium. Since it had not been established whether humans living in this seleniferous area developed a toxicosis of defined signs, a collaborative field study was carried out with the Antiepidemic Station and People's Hospital of the Enshi Region (Beijing Enshi Collaborative Survey Group, unpublished observations). This survey enabled us to obtain more information about the selenium status of residents in this area and the circumstances contributing to the outbreak of this intoxication.

It thus appears that two endemic human diseases associated with selenium occur in China. The first, described elsewhere, is a cardiomyopathy known as Keshan disease and is associated with selenium deficiency (2, 3). The second, described here, is associated with selenium intoxication and forms the basis of this report.

Experimental

Selenium analysis

Samples obtained in 1966 were analyzed by the method of distillation and titration (4). The rest of the samples were analyzed by the microfluorometric technique of Watkinson (5) with some modifications. Blood, hair, urine, water, and soil were digested in a mixture of sulfuric acid, perchloric acid, and sodium molybdate. Grains and vegetables were digested in a mixture of sulfuric, perchloric, and nitric acids. After digestion, 10% hydrochloric acid was added to samples from the seleniferous area to reduce all hexavalent selenium to tetravalent; however, results for grain and most vegetable samples from nonseleniferous areas were comparable whether hydrochloric acid was added or not. For water samples, hydrochloric acid must be added after digestion for complete reduction before determination of total selenium content. When 2,3-diaminonaphthalene was used in the reaction Se^{+4} as well as Se^{+6} content in ordinary water samples containing small amounts of organic matter could be measured differentially, depending on the addition or omission of hydrochloric acid. In soil samples, water-soluble selenium was extracted with deionized water on a boiling water bath.

Estimation of humus content

Humus in soil was extracted with pyrophosphate buffer in a boiling water bath and the amount was

calculated from the quantity of potassium dichromate reduced (6).

Dietary selenium intake

Two kinds of sites in the seleniferous area were surveyed. One was a high-selenium area where selenosis was common in livestock and signs of selenosis in particular deformation of nails sometimes occurred in humans. The other was a high selenium area in which selenosis has never appeared in either humans or livestock. After information was obtained regarding the dietary habits of the subjects observed, typical staple cereals and vegetables were collected from each family for selenium analysis and the daily dietary selenium intake was calculated.

Results

Human selenium intoxication during peak prevalence

The tissues most affected during the time of heavy prevalence were hair, finger and toe nails, skin, possibly teeth, and the nervous system. Selenosis was diagnosed by loss of hair and nails.

Loss of hair and nails. The hair becomes dry and brittle and is easily broken off at the scalp. The appearance of a rash on the scalp is associated with intolerable itching. Usually hair can be removed by hard scratching. When hair is broken off, the radicles remain intact so that the hair continues to grow. Hair may also be lost from the brow, beard, arm pit, and pubic area. New hair is always depigmented and loses its luster; sometimes the ends are forked.

The nails **(Fig 2)** become brittle, and white spots and longitudinal streaks appear on the surface, followed by a break on the wall of the nail. Thumbs are always affected first. As new growth continues, the broken nail is pushed forward and finally drops off. This process may require 1 month to complete. In many cases, fluid effuses from the skin around the nail. In those cases, a much longer period is needed to finish the whole process. The new nail is fragile and thickened, and its surface is rough and stripped. Repeated attacks may result in acropachia (clubbing of the fingers).

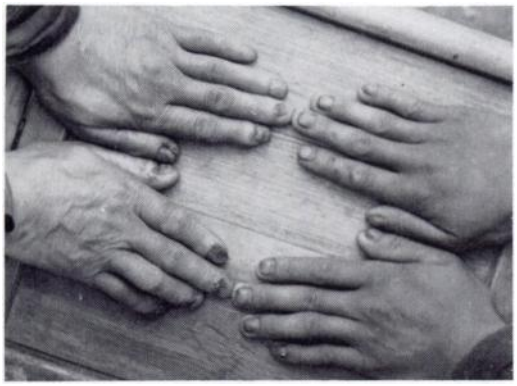

FIG 2. Loss of nails of patients during peak prevalence.

Skin lesions. Skin lesions occur mainly on the four limbs, ie, the back of hands and feet, the outer side of legs and thighs, the forearms and the back of the neck. Affected skin becomes red and swollen and then blistered and eruptive. In some cases ulcerations follow that take a long time to heal. Reddish pigmentation of the skin usually remains and gooseflesh may be left on the neck and thighs.

Tooth decay. Nearly one-third of 66 cases had mottled teeth and in a few cases the teeth were erosive or had pits. Since there was some fluorosis reported in this area, it could not be decided whether the tooth damage was caused by the fluoride or selenium alone or by a combination of the two. However, there is some evidence (7) from a number of studies that excessive exposure to selenium increases dental caries in men and animals.

Nervous system. Abnormalities of the nervous system were observed only in one heavily affected village with 18 cases of selenosis among 22 inhabitants. Initially the patients may complain of peripheral anesthesia, "pins and needles," acroparaesthesia, and pain in the extremities. Hyperreflexia of the tendon is common, and then numbness, convulsions, paralysis, motor disturbance, and even hemiplegia may develop. It is likely that all clinical neurological signs are due to polyneuritis caused by intoxication. Among those 18 patients, three had paresthesia and one hemiplegic died. Disturbances of the digestive tract usually accompanied this type of intoxication.

Case report. The hemiplegic was a female in her 40s. The hemiplegia progressed slowly and involved both motor and sensory abnormalities. Initially she had a sour taste, loss of appetite, bad headaches, dizziness, vertigo, peripheral anesthesia, and numbness in addition to pain in her scalp and fingers. General muscle weakness and an increased tendon reflex were present early. Her mental

TABLE 1
Selenium levels of hair, blood, and urine of residents living in high-, adequate- and low-selenium areas*

Place	Hair		Blood		Urine	
	n	Se content	n	Se content	n	Se content
		μg/g		μg/ml		μg/ml
High selenium area of chronic selenosis	65	32.2 (4.1–100)	72	3.2 (1.3–7.5)	17	2.68 (0.88–6.63)
High selenium area without selenosis	14	3.7 (1.9–8.2)	14	0.44 (0.35–0.58)	14	0.14 (0.04–0.33)
Selenium adequate area	1745	0.36 ±0.17	111	0.095 ±0.091	19	0.026 ±0.012
Low selenium area	40	0.16 ±0.04	40	0.027 ±0.009		
Low selenium area with Keshan disease	1478	0.074 ±0.050	173	0.021 ±0.010	43	0.007 ±0.001

* Mean ± SD or range shown in parentheses.

status was diminished. No autopsy was performed so the actual cause of the hemiplegia could not be determined. No clinical history of her previous background of illness was available.

Selenium status of residents in areas of chronic selenosis during sampling in 1966, 1978, and 1979 after the peak prevalence had subsided

Selenium levels in hair, blood, and urine. The average hair selenium content of residents in the high selenium area with chronic selenosis was about eight times that in the high selenium area without selenosis, 100× that in the selenium adequate area, and 400× that in the Keshan disease area. The samples from the last area were collected from 1972 to 1981 **(Table 1)**. One hair sample from the chronic selenosis area that reached a value of 100 μg/g was thought to be contaminated by coal smoke (see below).

The blood selenium levels in the high selenium area of chronic selenosis were markedly elevated, even after the peak prevalence of the disease. The average concentration was about 30× that in the selenium adequate area and 160× that in the Keshan disease area. The highest value, 7.5 μg/ml, exceeds the critical level our experimental animals can tolerate and is about 1000× as high as the average value, 0.008 μg/ml, in a certain Keshan disease area (Shanxi province). Such extremely high values suggest the possibility of an adaptive mechanism in humans exposed to high selenium intakes. Adaptation of microorganisms and rats to higher levels of selenium has already been reviewed by Levander (8).

TABLE 2
Selenium content of vegetables from the high selenium area of chronic selenosis*

Vegetable	Selenium content
	μg/g
Brassica pekinensis rupt	36.4 (5.8–72.2)
Turnip	12.0
Turnip, green	457 (24, 891)
Red pepper	22.8 (5.8–40.6)
Garlic, green	44.8 (8.3, 81.4)
Chinese onion	22.9 (12.4–29.8)
Leeks	63.0
Colza, large	3.7
Carrot	11.8
Carrot, green	24.2
Egg plant	38.3
Pumpkin	33.2 (6.3, 60.0)
Ginger, foreign	7.8 (3.4–13.2)
Flat bean	37.2
Cow pea, fresh	23.8 (2.0–47.5)
String bean	28.2
Sweet potato	9.2 (3.2–15.1)
Potato	2.0 (0.3–5.0)

* Dry basis; values of two samples or range shown in parentheses.

As was the case for hair and blood, the urinary selenium content tended to reflect the degree of selenium exposure in different areas.

Selenium levels in foods and total diet. Vegetables taken from the area of chronic selenosis contained large amounts of selenium **(Table 2)**. The selenium level in a given species of vegetable sampled from different locations varied greatly. Turnip greens were suspected as especially important in this particular episode of human selenosis, because

they are very popular with the inhabitants, and very high in selenium. The average selenium content of turnip greens from this area was more than 45,000× the average selenium content of 21 kinds of vegetables taken from a Keshan disease area (0.01 μg/g). Other vegetables from the selenosis area, such as *Brassica pekinensis rupt*, garlic greens, leeks, pumpkin, egg plant, and beans may also be toxic to man if large amounts are consumed.

Selenium content also differed widely between cereals from the area of chronic selenosis and from a Keshan disease area **(Table 3)**. Corn, rice, and soybeans produced in the chronic selenosis area were about 1500, 500, and 1000× as high as those from the Keshan disease area. The selenium content of corn in the chronic selenosis area was higher than that in rice, even though corn generally contained less selenium than rice in the other areas. This may partly be due to contamination of the corn by seleniferous coal during drying before storage (see below).

The traditional diet of the Chinese peasant is basically vegetarian and includes mainly cereals, beans, and vegetables with only seasonal variations in the kind of each component. Shipment of foods from one region to another is not common in rural areas and the daily selenium intake is derived mainly from locally grown products. The average daily calculated selenium intake in the area of chronic selenosis was 4.99 mg with a range of 3.20 to 6.69 mg **(Table 4)**. Although this is approximately 43× the typical intake of healthy staff members at the Institute of Health at Beijing, one may question whether this intake, per se, could have been responsible for the intoxication or whether additional factors may have contributed. Still, as the significant correlations between levels of selenium in the hair of inhabitants and in staple foods demonstrate ($r = 0.826$, $p < 0.01$) the excessive concentrations are well reflected in this human tissue **(Table 5)**. The present agricultural policy encourages the peasants to produce many more kinds of crops and exchange foods at the market. That policy should help prevent various kinds of endemic

TABLE 3
Selenium contents of cereals and soybean grown on soils in areas with excess, adequate, and deficient selenium*

Place	Corn		Rice		Soybean	
	n	Se content	n	Se content	n	Se content
		μg/g		μg/g		μg/g
High selenium area of chronic selenosis	44	8.1 (0.5–28.5)	22	4.0 (0.3–20.2)	17	11.9 (5.0–22.2)
High selenium area without selenosis	2	0.57	2	0.97	2	0.34
Selenium adequate area	82	0.036 ±0.056	76	0.035 ±0.027	31	0.069 ±0.076
Low selenium area	10	0.009 ±0.009	32	0.022 ±0.009		
Low selenium area with Keshan disease	195	0.005 ±0.003	49	0.007 ±0.003	150	0.010 ±0.008

* Mean ± SD or range shown in parentheses.

TABLE 4
Daily selenium intake of residents living in high-, adequate-, and low-selenium areas

Place	n	Daily selenium intake			Se intake from staple cereals as % of total daily intake
		Minimum	Maximum	Average	
		mg	mg	mg	
High selenium area of chronic selenosis	6	3.20	6.69	4.99	28–70
High selenium area without selenosis	3	0.24	1.51	0.75	25–45
Selenium adequate area (Beijing)	8	0.042	0.232	0.116	Various sources
Low selenium area with Keshan disease	13	0.003	0.022	0.011	Mainly from cereals

diseases of geochemical origin, such as selenosis or Keshan disease.

Environmental sources of selenium. The water-soluble portion of the soil selenium should represent the amount available for uptake by plants. Several factors, such as total soil selenium content, humus and iron content, and soil pH could influence the quantity of selenium released into the water. In different regions, those factors could act in different combinations to create areas that are excessive, adequate, or deficient in selenium.

The total selenium content of soil samples from Enshi, a selenosis region, was more than 100× that from a Keshan disease region of Shandong province **(Table 6)**. Moreover, the amount of water-soluble selenium in soil from Enshi was about 80× that in soil from Shandong. There was a positive correlation between total and water soluble soil selenium content ($r = 0.985$, $p < 0.01$).

Humus may prevent soil selenium from being released into the water. For example, the total soil selenium content in Heilongjiang is about 3× that in Shandong, but the amount of water-soluble selenium is about one-third less. There is a negative correlation between the humus content and the percentage of selenium released ($r = -0.463$, $p < 0.01$). That factor may be important in the etiology of selenium deficiency in those areas where the total soil selenium content is low, such as certain provinces in northeastern China. The effect of soil pH is shown by the samples from Chengdu (pH = 6.4) and Heilongjiang (pH = 6.3) both of which had less water soluble selenium than the sample from Beijing (pH = 8.0). The traditional application of lime as fertilizer in Enshi would raise the pH of soil, thus facilitating the oxidation of Se to the selenate state.

There is good correlation ($r = 0.830$, $p < 0.01$) between the selenium content of cereals and soybeans and the amount of water-soluble selenium in the soil **(Table 7)**. The correlation shows that the regional differences in the selenium concentration in crops reflect the uneven distribution of selenium in the soil.

Drinking water generally contributes insignificantly to the daily selenium intake, but in the chronic selenosis area the average selenium concentration of 11 samples was 54 μg/1. Of these samples, four were surface water from a village with a previous heavy prevalence of selenosis and these averaged 139 (117 to 159) μg/1. Such water would no doubt contribute to the high selenium intake, but

TABLE 5
Relationship between selenium content of hair of residents from different areas and the selenium content of the staple foods consumed*

Sampling site	Selenium content (μg/g)		
	Hair	Corn	Rice
Enshi, Hubei	23.34 ± 2.56 (15)	6.330 (5)	1.483 (4)
Fushu, Xinjiang	0.860 ± 0.031 (10)	0.286 (1)	0.145 (1)
Tiandeng, Guangxi	0.482 ± 0.016 (20)	0.146 (2)	0.095 (2)
Lingan, Zhejiang	0.405 ± 0.011 (18)		0.048 (2)
Longhai, Fujian	0.233 ± 0.030 (20)		0.047 (2)
Huanglong, Shanxi	0.076 ± 0.008 (22)	0.005 (2)	
Shangzhi, Heilongjiang	0.075 ± 0.006 (20)	0.004 (4)	0.024 (25)
Miangning, Sichuan	0.071 ± 0.003 (20)		0.009 (2)
Nanhua, Yunan	0.068 ± 0.004 (20)	0.004 (3)	0.004 (3)

* Mean ± SE; numbers in parentheses are the number of samples analyzed.

TABLE 6
Relationship of total soil selenium and humus contents to the amount of water soluble selenium in soil*

Sampling site	Total soil selenium	Soil humus content	Water soluble selenium in soil	
			μg/100 g	% total selenium
	μg/100 g	%		
Enshi, Hubei (6)	787 ± 69	2.35 ± 0.09	35.4 ± 4.5	4.3 ± 0.4
Chengdu (8)	31.8 ± 1.6	1.19 ± 0.14	1.1 ± 0.2	3.5 ± 0.4
Beijing (7)	28.1 ± 2.4	0.93 ± 0.09	3.9 ± 0.5	14.0 ± 1.2
Heilongjiang (6)	18.2 ± 1.7	1.77 ± 0.13	0.33 ± 0.03	1.9 ± 0.3
Sichuan (12)	8.4 ± 1.1	1.43 ± 0.18	0.28 ± 0.03	3.1 ± 0.5
Shandong (12)	5.9 ± 0.7	0.36 ± 0.06	0.44 ± 0.05	7.8 ± 0.4

* Mean ± SE; numbers in parentheses are the number of samples analyzed.

TABLE 7
Relationship between amount of water soluble selenium in soil and selenium content of crops grown thereon*

Sampling site	Selenium content in soil		Selenium content of crops			
	Total	Water soluble	Corn	Wheat	Rice	Soybean
	μg/100 g		μg/100 g			
Enshi	787	35.4	633 (5)		148 (4)	
Chengdu	31.8	1.1	1.36 (2)	6.06 ± 1.01 (4)	2.99 ± 0.24 (4)	3.48 (2)
Beinjing	28.1	3.9	2.26 ± 0.21 (7)	3.82 ± 0.66 (7)	4.12 ± 0.31 (11)	7.58 ± 1.37 (6)
Heilongjiang	18.2	0.33	0.36 ± 0.02 (76)	0.61 ± 0.06 (21)	2.26 ± 0.19 (26)	0.77 ± 0.06 (54)
Sichuan	8.4	0.28	0.32 ± 0.04 (16)	0.59 ± 0.07 (20)	0.57 ± 0.05 (18)	0.61 ± 0.04 (24)
Shandong	5.9	0.44	0.98 ± 0.03 (19)	1.30 ± 0.09 (21)		2.60 ± 0.15 (25)

* Mean ± SE; numbers in parentheses are the number of samples analyzed.

drinking water is still far less important a source than the diet. The other seven drinking water samples came from a variety of sources and they averaged only 5 μg/1. Speciation studies indicated that selenium in the water from this region was almost totally in the hexavalent state.

The average selenium content of 10 coal samples collected from the selenosis area of China in 1966 was 291 μg/g (range 128 to 834; one sample of 3632 was excluded). The selenium content of another 9 samples collected from the same area in 1978 was 367 μg/g (range 13 to 1332). A tenth sample from the 1978 survey assayed 84,123 μg/g. In a joint China-USA collaborative selenium analysis, that sample was sent to Prof Oscar E Olson's laboratory in South Dakota through the help of Dr OA Levander in Beltsville, MD and assayed 92,800 μg/g. To our knowledge, such a high content of selenium in coal has never previously been reported. The selenium content of coal samples in the USA generally runs between 1 and 2 μg/g (9). The seleniferous coals from Enshi clearly have great potential for contaminating the environment. The distribution of selenium in coal beds in that area is never uniform and varies not only from place to place but also from bed to bed. In this region the selenium usually is concentrated in the lower stony bed of the coal.

Selenosis in livestock

Alkali disease of cattle was not uncommon in the affected area. Pigs frequently showed inflammation of the feet or sloughing of the hoofs accompanied by loss of body hair. The selenium content of the hair of an intoxicated pig was 21.5 μg/g. Piglets usually wandered restlessly in circles, seeming to seek shelter such as a cave, and finally died.

TABLE 8
Selenium content of animal feedstuffs from the high selenium area of suspected selenosis*

Feedstuff	Selenium content
	μg/g
Sweet potato leaf	23.3 (7.8, 38.8)
Arstemisia spp	19.9 (2.9, 36.9)
Aster indicus L.	74.4 (20.6, 128.2)
Cirsium segetum Bge	86.6
Astragalus sinicus L	108 (64.3, 151.6)
Lichen	738

* Dry basis; range shown in parentheses.

Eggs produced in this area had very low hatchability. Even if the eggs hatched, the embryos were often deformed with ropy feathers and without beaks. One sample of eggs of low hatchability contained 3.6 μg/g of selenium (wet basis). Poor hatchability and inability to raise piglets seemed to be the most sensitive parameters for the detection of selenosis in this area.

Many of the feedstuffs analyzed contained very high levels of selenium (**Table 8**). It is no wonder that selenosis of livestock occurred frequently in this area. Lichen had a very high selenium content which supports the suggestion that this plant tends to concentrate selenium (10).

Selenosis in plants

Although it was suggested that plant injury due to selenium overexposure would proba-

bly not occur under natural conditions (9), injuries to plants did in fact occur in our seleniferous area, especially during the heavy prevalence years. Some leaves of injured soybeans and tomatoes were mottled with brown spots, and some became chlorotic. Although tobacco leaves showed yellow areas on the surface, the selenium concentration in the blade was not high, one sample containing 5.6 μg/g (dry basis). "White seedlings" might occur among corn plants. Leaf edges of injured corn usually became discolored and surfaces showed white streaks and the corn kernels stuck firmly to the cob.

Discussion

This report describes an outbreak of human selenium poisoning in Enshi County of Hubei Province in the People's Republic of China. The signs of human selenosis that we observed closely resembled those reported by Smith and coworkers (11, 12) in their earlier surveys of rural populations in seleniferous areas of Wyoming, South Dakota, and Nebraska in the USA in 1936. Those authors could not establish a direct relation between the signs they observed in humans and the ingestion of large amoungs of selenium because they could not show a definite association between clinical signs of individuals and the level of selenium in the urine. The urinary selenium concentrations reported by Smith and Westfall (11) in South Dakota and Nebraska ranged between 0.2 and 1.98 μg/ml. Even their maximum individual value is lower than our mean value of 2.68 μg/ml. The highest individual urinary selenium level reported by Jaffe et al (13) in a seleniferous area in Venezuela was 3.9 μg/ml which is still less than the maximum value of 6.63 μg/ml seen in our high selenium area with chronic selenosis. In our opinion, however, the urinary selenium level varies too much for use as a reliable criterion of selenium exposure.

In previous work we were successful in using hair and blood selenium levels to distinguish between populations that were deficient or adequate in selenium (see Table 1). It now seems likely that hair selenium level could also be used to test a given population for selenium intoxication in seleniferous areas, since the average hair selenium content decreased from 32.2 to 3.7 μg/g as the sampling site shifted from a high selenium area with selenosis to a nearby high selenium area without selenosis. Blood selenium levels also are useful for monitoring endemic selenium overexposure since they averaged 3.2 and 0.44 μg/ml in high selenium areas with and without selenosis, respectively.

Jaffe et al (13) concluded that selenium excess did not pose a serious health hazard when blood and urinary selenium levels of children in seleniferous areas did not exceed 0.813 and 0.636 μg/ml, respectively. Corresponding values in our high-selenium area without selenosis were 0.44 (0.35 to 0.58) μg/ml for blood and 0.14 (0.04 to 0.33) μg/ml for urine. Therefore, we believe that the selenium levels in samples of hair, blood, and urine collected in our high selenium area without selenosis were below the upper limit of safety. Howe (14) recently reported that the mean blood selenium levels in 34 different locations in South Dakota ranged from 0.22 to 0.32 μg/ml, which would also fall below the upper safe limit suggested by Jaffe et al (13).

Previous work by us indicated that the minimum safe hair and blood selenium levels characteristic of populations protected against selenium deficiency (Keshan disease) were 0.16 μg/g and 0.027 μg/ml, respectively (see Table 1). If we assume that the maximum tolerable levels of selenium in hair and blood were 3.75 μg/g and 0.44 μg/ml, respectively, then the ratio of maximum selenium level tolerated versus minimum selenium level required would be 23 for hair and 16 for blood. Apparently the margin of safety is adequate between potentially toxic and nutritionally required levels of selenium.

The average daily selenium intake of adults in the high selenium area without selenosis was estimated as 750 μg which is about 70× that in a selenium-deficient area with Keshan disease and more than double the intake reported in Caracas, Venezuela (15). Under normal conditions, human selenium poisoning caused by ingestion of locally produced, high selenium foods would be rare. The possibility of selenium deficiency seems more likely, particularly in those regions where the amount of available selenium in the soil is low. The data presented here suggest that the margin of safety is adequate for the supplementation of deficient diets with moderate amounts of selenium.

To determine the critical intake at which

intoxication occurs is more difficult. In our institute, a male worker, 62 yr old, believing that selenium would benefit his health, took one tablet of 2 mg sodium selenite per day for more than 2 yr, until he was warned that he had been intoxicated. He did not have any symptoms of indisposition but presented with thickened, fragile nails, and garlic odor in dermat excretions. After he stopped his oral sodium selenite, the surface of new nail growth became smooth and gradually recovered. Evidently, an intake of 1 mg Se daily from sodium selenite for a long time is definitely chronically toxic to humans. His blood and hair selenium concentrations were 0.179 and 0.828 ppm on the day he stopped his selenium intake. Therefore, determination of tissue selenium level alone is not adequate for the diagnosis of selenosis without differentiation of the forms of selenium ingested. These observations and those of others suggest that the behavior of organic selenium is different from inorganic. In our endemic selenosis area deformation of the nail may appear, and it is reasonable to assume that the daily dietary selenium intake of 4.99 mg is chronically toxic. This is five times the critical level of which selenite-selenium produced familiar types on the case reported above. The relation of the external signs (hair and nail loss) in selenosis to pathological changes of other tissues remains to be clarified. Also, potential influences from adaptation of the subjects to a high selenium environment and interactions of the latter with other nutritional and toxic agents require further study.

The ultimate environmental source of selenium in this high selenium area was coal. Weathering, leaching, and possibly biological action would mobilize selenium from the coal to the soil and thus make it available to the crops. The traditional use of lime fertilizer would also render the selenium accumulated in the soil more readily available to plants. Moreover, the unusually high selenium content of the coal might heavily contaminate the air or foodstuffs by its smoke and thus contribute additionally to the selenium intake of the residents. All of these conditions were responsible for the high selenium intakes of the residents in this seleniferous area, but additional factors were believed necessary to account for this particular outbreak of selenosis. For example, the drought at that time led to a failure of the rice crop which forced the villagers to consume more vegetables and maize instead. The vegetables usually contained very high levels of selenium as compared with rice (up to 70% of the selenium intake could have come from vegetables, see Table 3). Furthermore, maize grown on dried out paddy fields accumulated substantially more selenium than the rice crop normally grown (Table 3). Local peasants used large amounts of plant ash to increase the yield of farm products during those years; thus it is possible that considerable amounts of selenium could have been returned to and concentrated in the soil. Finally, the residents consumed fewer protein foods because of the crop failure and therefore would likely be more sensitive to the toxic action of excessive selenium intake (16).

The exact extent of this seleniferous region in China is unknown. During the heavy prevalence years intoxicated residents were found only in six communes. However, another seleniferous area north of Enshi was recently reported in Ziyang County, Shanxi Province (17). The reported selenium content of some coal samples in that county was more than 30 μg/g and the highest hair selenium content of commune members was 58 μg/g. The distribution pattern of isolated seleniferous areas in this region most likely follows the pattern of the coal bed. Do many isolated seleniferous areas exist in this region? If so, why are high selenium foods produced only in a very limited area in Ziyang county in contrast with its more widespread distribution of high selenium stony coal? These interesting questions are worthy of study by geologists.

References

1. Yang GQ. Research on the etiology of an endemic disease characterized by loss of nails and hair in Enshi county. A preliminary report to the research office of the Chinese Academy of Medical Sciences, March, 1966.
2. Keshan Disease Research Group. Observations on effect of sodium selenite in prevention of Keshan disease. Chin Med J 1979;92:471–6.
3. Keshan Disease Research Group. Epidemiologic studies on the etiologic relationship of selenium and Keshan disease. Chin Med J 1979;92:477–82.
4. Rosenfeld I, Beath OA. Selenium: geobotany, biochemistry, toxicity and nutrition. New York, NY: Academic Press, 1980.

5. Watkinson JH. Fluorometric determination of selenium in biological material with 2,3-diaminonaphthalene. Anal Chem 1966;38:92–7.
6. Physico-chemical analysis of soil. Nanjing Institute of Soil, 1978.
7. Hadjimarkos DM. Selenium in relation to dental caries. Food Cosmet Toxicol 1973;11:1083.
8. Levander OA. Metabolic interrelationships and adaptations in selenium toxicity. Ann NY Acad Sci 1972;192:181.
9. Committee on Medical and Biologic Effects of Environmental Pollutants. Selenium. Washington, DC: National Academy of Sciences, 1976.
10. Reimers E, Gaare E, Skjenneberg S. Selenium content in lichen in Lapland and South Finland and its effect on the selenium values in reindeer. Rros, Norway: Proc 2nd Int Reindeer/Caribou Symp, 1979.
11. Smith MI, Westfall BB. Further field studies on the selenium problem in relation to public health. US Public Health Service Public Health Rep 1937;52:1375–84.
12. Smith MI, Franke KW, Westfall BB. The selenium problem in relation to public health. US Public Health Service Public Health Rep 1936;51:1496–505.
13. Jaffe WG, Ruphael MD, Mondragon MC, Cuevas MA. Biochemical and clinical studies on school children in a seleniferous zone. Arch Latinoamer Nutr 1972;22:595–611.
14. Howe M. Selenium in the blood of South Dakotans. Arch Environ Health 1979;36:444–8.
15. Mondragon MC de, Jaffe WG. Ingestion of selenium in Caracas, compared with some other cities. Arch Latinoam Nutr 1976;26:341–52.
16. Rosenfeld I, Beath OA. The influence of protein diets on selenium poisoning I. Am J Vet Res 1946;7:52.
17. Chen JE, Mei QJ. A preliminary report of a seleniferous area in Ziyang County, Shanxi. Nongye Kexue 1980;6:17.